Genetic Material and Introduction

Introduction

DNA is the storage form of all information for all cells throughout the entire body. Every cell has the same DNA sequence. They're genetic clones of a single fertilized egg. And yet, from that one cell come all the different cells in the body. They all have the same genetic code, but each expresses the code differently. A cardiac myocyte contracts, a neuron depolarizes, and a β cell of the pancreas secretes insulin.

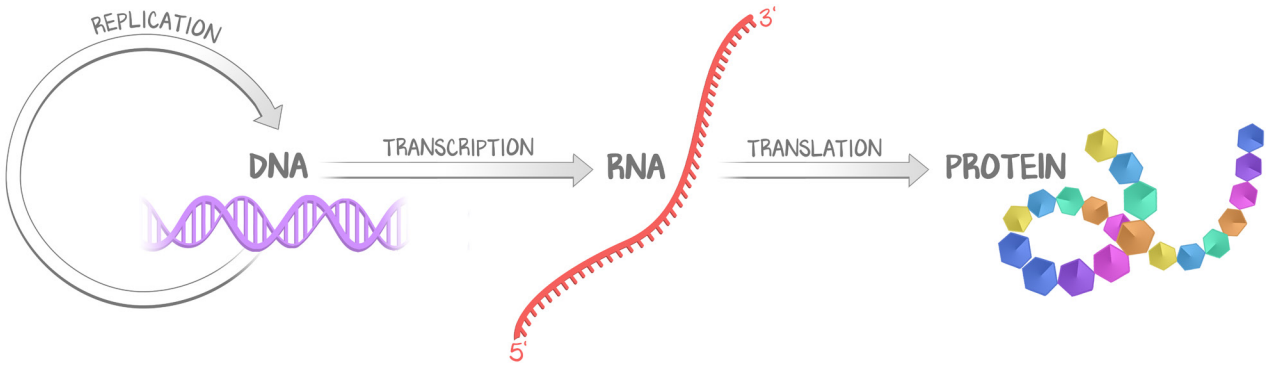

Figure 1.1: Overview
DNA exists to copy itself for replication. Then that DNA holds the code to be transcribed into RNA, which is then translated into amino acids, and finally, those amino acid chains are mainpulated into complete proteins.

When a cell needs to proliferate, it must copy all of the genetic material through a process called **replication**. Everything that a cell does, every protein expressed or made, any ligand secreted, any receptor inserted, is mediated by the nucleus. From that one sequence of code comes an infinite possibility of function. When cells do what they do, they don't copy the entirety of genetic material. Instead, the cells access certain parts of the genetic material that codes for the thing it needs, a process called **transcription**. The **RNA copy** of the DNA, the transcript, is sent from the nucleus to the cytoplasm where ribosomes then **translate** it into protein. The DNA in the nucleus becomes RNA from the nucleus, which becomes an amino acid sequence in the cytoplasm (or the endoplasmic reticulum).

The entirety of all the genes in you simultaneously exists in every cell, and yet expression of those genes in different cells is strikingly different. It's because the nuclear material is packaged in a certain way that allows for economy of space—the entire genetic sequence fits inside the nucleus, an organelle within a functioning cell—but also allows certain genetic material to be accessed on demand.

DNA can be safely **packaged** for storage and also unraveled so as to be **accessible**.

PACKAGED	ACCESSIBLE
Safe from degradation	Vulnerable to degradation
Lots in a small space	Less in a small space
Helicase	Able to be transcribed or replicated

Table 1.1

Prokaryotic DNA (No Packaging)

Circular DNA is the default DNA structure. Circular (effectively unpackaged) DNA usually exists in plasmids, bacteria, or mitochondria. Circular DNA has no economy of space. It's also very readily accessible. This type of uncoiled, unpackaged DNA is easily transcribed, replicated, and denatured. Thus, it's utilized by less-sophisticated organisms. The bacteria cell has to do only one cell's work; it has no need for the possibility of millions of potential products from that code. There isn't the stress of many different functions—that bacterial cell will only be a bacterium and its DNA need never code for anything else.

Supercoiling

Eukaryotic nuclei take advantage of a process called **supercoiling**, which allows circular DNA to be wound tightly by twisting that circular DNA. This eliminates much of the in-between space and packs the DNA tightly together.

Negative supercoiling is when the DNA is more loosely coiled than Watson-Crick DNA. **Positive supercoiling** is when the DNA is tighter than Watson-Crick DNA. Topoisomerases cause transient nicks in the phosphate-pentose backbone, then reseal them, with positioning of the nuclear material in a more or less efficient form.

Histones and Nucleosomes

Additionally, **histones** allow for supercoiled DNA to be further "wound up." **Histones** are **positively charged** (rare for amino acids) because of a high density of positively charged amino acids such as arginine and lysine. As we will learn, double-stranded DNA has a **negatively charged pentose-phosphate** backbone. Histones, being positively charged, can easily interact with (and bind to) **DNA**.

A **nucleosome** is a **10-nm** structure, a combination of a histone complex and coiled DNA around it. The **histone octamer** consists of two copies of each histone, H2A, H2B, H3, and H4, symmetrical top and bottom. This maximizes the histone-DNA interaction, acting like a shoelace and drawstring. The supercoiled DNA gets wrapped around the histone octamer. This particular structure **lacks histone H1**. Without H1, the packing is "only 10 nm," and not as tightly packed as it could be. Supercoiling makes circular DNA tight.

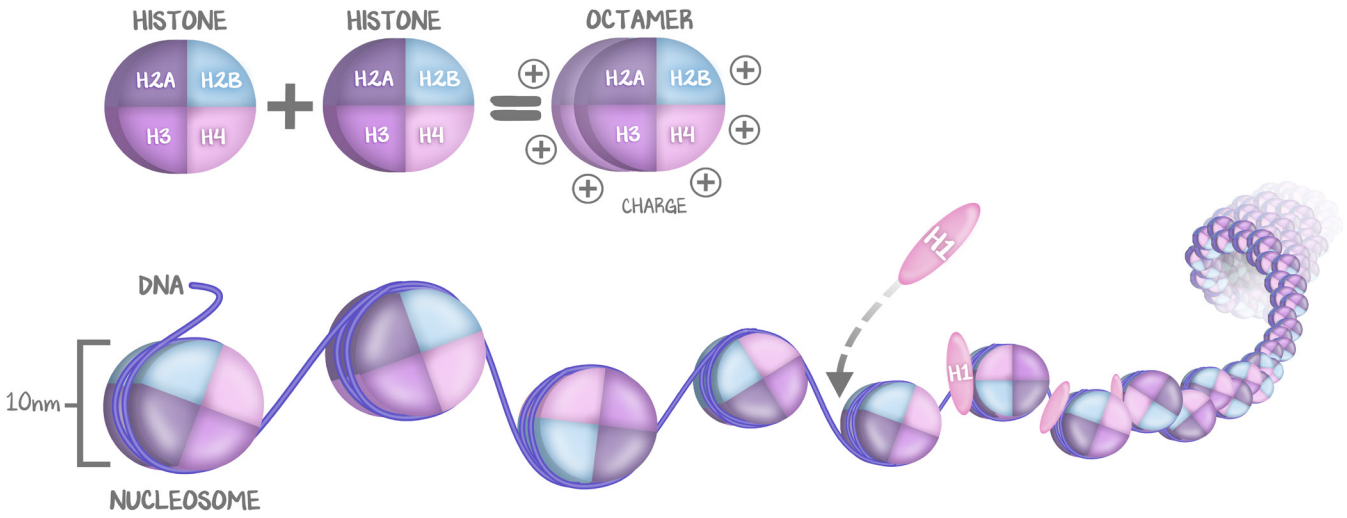

Figure 1.2: Histones and Nucleosomes
Histones comprise 8 total subunits, four of the same subunit duplicated. These octamers are rich in lysine and arginine, which give a positive charge to the octamer, allowing it to easily interact with DNA, binding it closely. The combination of the histone octamers with the DNA forms the 10-nm nucleosome.

Histones can interact with supercoiled DNA, but it's the octamer of histones that maximizes that coiling. Add **histone H1** to get the maximal tight packaging. With the H1 histone present, the fibers will pack into 30-nm fibers.

Beyond that, scaffolding proteins make more-complex higher-order packaging (the details here are intentionally omitted).

Euchromatin and Heterochromatin

When a cell **isn't replicating** (it's not copying all of its genetic material and dividing into two), but instead making protein, expressing genes, and transcribing according to its active interphase needs, its DNA will exist in two forms. The **euchromatin** is the loosely wound, accessible form which is seen on electron microscopy as thin black lines within the nucleus. Loosely packed, histone H1-lacking DNA is the type of DNA that is susceptible to degradation as well as accessible to transcription and replication.

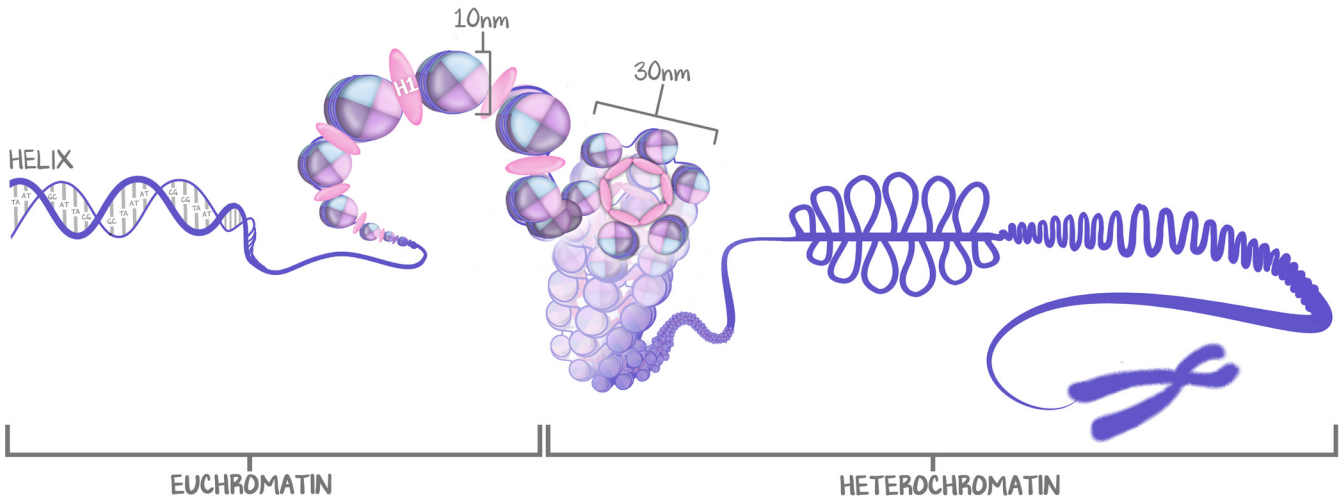

Figure 1.3: Overview, DNA Packaging
Starting with the double-helix structure on the far left, the DNA is wound about histone octamers to form the 10-nm fibers of the nucleosomes. When histone H1 is added, this combination of octamers and DNA results in the 30-nm fiber. These fibers can be further and further condensed with less-specified but more-sophisticated packaging. The metaphase chromosome, the pairing of two sister chromatids into the butterfly-shaped X pattern on the far right, is the most densely packed DNA there is.

Euchromatin is accessed for gene expression and transcription. **Heterochromatin** is the tightly wound, inaccessible DNA. Genetic code in heterochromatin is not undergoing gene expression or transcription. This makes this section of DNA extremely **dense**. The dense region of DNA is referred to **heterochromatin**, insensitive to degradation and also inaccessible to transcription or replication. The hepatocyte may never need the code for a red blood cell, and so the red blood cell section of code can be packed safely away in heterochromatin.

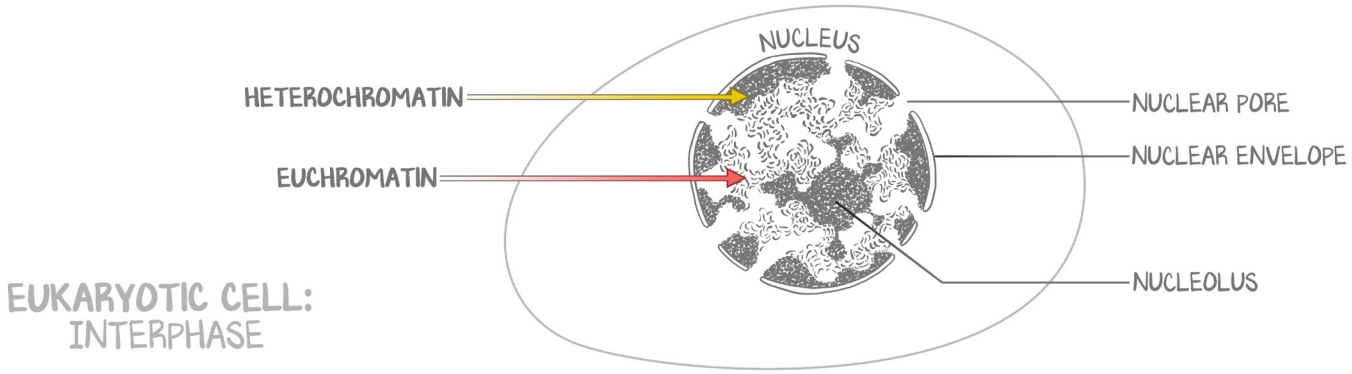

Figure 1.4: Euchromatin and Heterochromatin
Electron microscopy of an interphase cell. Here we can see the densely packed heterochromatin (inaccessible to transcription) as well as euchromatin (loosely packed and accessible to transcription). Other features demonstrated are the nuclear pores that allow mRNA out of the nucleus, the nuclear envelope which is a lipid bilayer, and the dense central circular nucleosome.

The most condensed that DNA can get is **active cell division replication**. There's effectively **no gene expression**, save only the proteins required to allow for replication and cell division. It's the most condensed DNA form in a eukaryotic cell and is presented to us as "chromosomes" in karyotyping.

Nuclear Membrane

The nucleus has a **lipid bilayer** just as the cell membrane does. It keeps DNA safe from degradation and ensures that only a complete, processed mRNA will be allowed out into the cytoplasm. It has **nuclear pores** that permit these mRNAs out into the cytoplasm. This also ensures that only very specific and intentionally dispatched **transcription factors** can ever even enter the region where DNA is, allowing for stricter regulation.